In the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently amended) A method of rejuvenating a mammalian primary cell, comprising:

a. transferring a mammalian primary cell, the nucleus from said primary cell or chromosomes from [[a]] said mammalian primary cell to a recipient enucleated oocyte or enucleated egg in order to generate an embryo, wherein

the mammalian primary cell and the recipient oocyte or egg are derived from the same mammalian species, and

said mammalian primary cell is a senescent cell or a cell that is near senescence;

b. obtaining an inner cell mass, embryonic disc and/or stem cell using said embryo;

c. injecting said inner cell mass, embryonic disc and/or stem cell into an immune-compromised animal to form a teratoma;

d. isolating said resulting teratoma;

e. separating the different germ layers for the purpose of identifying specific cell types;

f. isolating a cell of the same type as the mammalian primary cell, wherein the remaining number of population doublings of the isolated cell is greater than the remaining number of population doublings of said mammalian primary cell.

2. (Canceled) ~~The method of Claim 1, wherein said primary cell is a senescent cell or a cell that is near senescence.~~

3. (Currently amended) The method of Claim 1, wherein said cell isolated from said nuclear transfer teratoma has telomeres that are on average at least as long as those of cells from a same age control teratoma ~~that is~~, wherein said control teratoma is derived from cells that are not generated by nuclear transfer techniques.

4. (Currently amended) The method of Claim [[4]] 3, wherein said telomeres are on average longer than those of the cells from [[a]] the same age control teratoma ~~that is not generated by nuclear transfer techniques~~.

5. (Currently amended) The method of Claim [[2]] 1, wherein said primary cell is a fibroblast.

6. (Original) The method of Claim 1, wherein said immune-compromised animal is a SCID or nude mouse.

7. (Currently amended) The method of Claim 1, wherein said primary cell of step (a), prior to transfer, includes ~~has~~ at least one alteration to ~~the~~ its genome.

8. (Currently amended) A method of making a **mammalian** primary cell having the same genotype as a first **mammalian** cell which is of a different cell type, comprising:

a. transferring the nucleus from said first **mammalian** cell to a recipient **enucleated** oocyte in order to generate an embryo**, wherein**

the first mammalian cell and the recipient oocyte are derived from the same mammalian species, and

said first mammalian cell is a senescent cell or a cell that is near senescence;

b. obtaining an inner cell mass, embryonic disc and/or stem cell using said embryo;

c. injecting said inner cell mass, embryonic disc and/or stem cell into an immune compromised animal to form a teratoma;

d. isolating said resulting teratoma;

e. separating the different germ layers for the purpose of identifying specific cell types;

f. isolating a cell of a different type than the first **mammalian** cell, wherein the telomeres of said ~~new primary~~ **isolated** cell are at least as long **as** the telomeres of a ~~same age control~~ cell [[in]] **from** a **same age control** teratoma**, wherein the control teratoma is derived from cells that are** not generated by nuclear transfer techniques.

9. (Canceled) ~~The method of Claim 8, wherein said first cell is a senescent cell or a cell that is near senescence.~~

10. (Currently amended) The method of Claim [[9]] 8, wherein said first cell is a fibroblast.

11. (Original) The method of Claim 8, wherein said primary cell is of a type selected from the group consisting of smooth muscle, skeletal muscle, cardiac muscle, skin and kidney.

12. (Original) The method of Claim 8, further comprising growing said cell of a different type in the presence of growth factors to facilitate further differentiation.

13. (Currently amended) The method of Claim 11, wherein said primary cell is used to generate a tissue [[()] intended for transplantation into a patient in need of a transplant [[)]].

14. (Currently amended) The method of Claim 8, wherein the genome of the first mammalian cell of step (a), prior to transfer, includes at least one alteration ~~is altered prior to nuclear transfer~~.

15. (Original) The cell isolated by the method of Claim 8.

16. (Original) The tissue isolated by the method of Claim 13.

17. (Original) The method of Claim 7, wherein said genetic alteration comprises the transfection of at least one heterologous gene.

18. (Original) The method of Claim 7, wherein said genetic alteration comprises the disruption of at least one native gene.

19. (Original) The method of Claim 14, wherein said genetic alteration comprises the transfection of at least one heterologous gene.

20. (Original) The method of Claim 14, wherein said genetic alteration comprises the disruption of at least one native gene.

21. (Currently amended) A method of performing compound genetic manipulations in a mammalian primary cell, comprising rejuvenating said mammalian primary cell between genetic manipulations using nuclear transfer into a recipient mammalian enucleated oocyte, wherein said mammalian primary cell is passaged to a senescent or near-senescent state prior to nuclear transfer, and wherein said mammalian primary cell and said recipient mammalian oocyte are derived from the same mammalian species.

22. (Currently amended) A method of performing compound genetic manipulations in a mammalian primary cell, comprising rejuvenating said mammalian primary cell between genetic manipulations using nuclear transfer into a recipient mammalian enucleated oocyte, wherein said mammalian primary

cell is induced into a senescent-like or near-senescent-like state prior to nuclear transfer, and wherein said mammalian primary cell and said recipient mammalian oocyte are derived from the same mammalian species.

23. (Original) The method of Claim 21, whereby rejuvenation results in an embryonic cell that has telomeres at least as long on average as a same age control embryonic cell.

24. (Currently amended) A mammalian primary cell that has been genetically altered according to the method of Claim 21.

25. (Currently amended) A method of making a genetically altered mammalian animal having the same genotype as the cell of Claim 24, comprising

a. transferring the nucleus of said mammalian primary cell of claim 24 into a recipient enucleated oocyte, wherein said mammalian primary cell and said recipient oocyte are derived from the same mammalian species,

b. generating an embryo or embryonic stem cell from said nucleated oocyte,

c. introducing said embryo or embryonic stem cell into a recipient mammalian female, wherein said recipient female is the same mammalian species as said embryo or embryonic stem cell, and

d. allowing said embryo or embryonic stem cell to fully develop such that said female delivers a newborn

animal having the same genotype as said ~~primary~~ cell of claim 24.

26. (Original) The genetically altered animal produced by the method of Claim 25, whereby said animal has telomeres that are at least as long on average as a same age control animal.

27. (Currently amended) A method of re-cloning a cloned mammalian animal using nuclear transfer techniques, the method comprising:

a. transferring a nucleus of a donor cell from said cloned mammalian animal into a recipient enucleated oocyte, wherein the recipient oocyte is derived from the same mammalian species as the cloned mammalian animal;

b. generating an embryo or embryonic stem cell from said nucleated oocyte;

c. introducing said embryo or embryonic stem cell into a recipient mammalian female, wherein said recipient female is the same mammalian species as said embryo or embryonic stem cell; and

d. allowing said embryo or embryonic stem cell to fully develop such that said female delivers a newborn animal having the same genotype as said donor cell, wherein the donor cell used to supply the nucleus of the re-clone is a cell that is senescent or near senescence.

28. (Original) The method of Claim 25, wherein said re-cloned animal has been genetically altered with respect to the cloned animal.

29. (Currently amended) A method of making a re-cloned inner cell mass, blastocyst, teratoma embryo, fetus or animal containing at least two genetic modifications, comprising:

a. obtaining a primary cell from a mammalian animal of interest,

b. making a first genetic modification to said primary cell by inserting heterologous DNA and/or deleting native DNA,

c. allowing said genetically modified primary cell to multiply to senescence or near-senescence,

d. using a first genetically modified senescent or near-senescent cell as a nuclear donor for nuclear transfer to an enucleated oocyte or an enucleated fertilized egg, wherein the enucleated oocyte or the enucleated fertilized egg is derived from the same species as the mammalian animal of interest,

e. obtaining a cloned inner cell mass, blastocyst, teratoma, embryo, fetus or animal having said first genetic modification,

comprising steps where said re-cloned inner cell mass, blastocyst, teratoma, embryo, fetus or animal is again re-cloned, and wherein a third genetic modification is made such that the further re-clone has the first, second and third genetic modifications.

31. (Original) The method of Claim 30, wherein said further re-clone is generated by nuclear transfer techniques using a senescent or near-senescent donor cell.

32. (Currently amended) The method of Claim 29, wherein said re-clone has telomeres that are at least as long on average as a same age control animal ~~that was~~, **wherein said control animal was derived from cells that are** not generated using nuclear transfer techniques.

33. (Currently amended) The method of Claim 31, wherein said further re-clone has telomeres that are at least as long on average as a same age control animal ~~that was~~, **wherein said control animal was derived from cells that are** not generated using nuclear transfer techniques.

34. (Original) The method of Claim 29, wherein the genetic modifications involve genes that are responsible for immunological function.

35. (Original) The method of Claim 29, wherein said animal of interest is an ungulate.

36. (Original) The method of Claim 35, wherein said animal of interest is a bovine.

37. (Original) A method of re-setting the lifespan of senescent or near-senescent cells, comprising transferring the nucleus of said cell into a recipient oocyte.

38. (Original) The method of Claim 37 wherein said recipient oocyte is of a different species than said senescent or near-senescent cell.

39. (Original) The method of Claim 37 further comprising generating an embryo or embryonic stem cell from said nucleated oocyte.

40. (Withdrawn) A method of identifying at least one gene that either directly or indirectly enhances telomerase activity, comprising, screening a cDNA or mRNA library generated from an embryo or embryonic stem cell for members that enhance telomerase activity in a senescent or near-senescent cell.

41. (Withdrawn) The method of Claim 40 whereby enhancement in telomerase activity is measured by measuring for enhanced expression of a telomerase reporter gene.

42. (Withdrawn) The method of Claim 41 wherein said telomerase reporter gene is a construct comprising the hart gene fused to a reporter gene.

43. (Withdrawn) The method of Claim 42 wherein the construct comprises a gene fusion.

44. (Withdrawn) The method of Claim 42 wherein the construct comprises a protein fusion.

45. (Withdrawn) The method of Claim 40 whereby enhanced telomerase activity is measured via the TRAPeze assay.

46. (Withdrawn) The method of Claim 40 whereby said cDNA or mRNA library is subjected to subtractive hybridization with a cDNA or mRNA library from a senescent cell prior to library screening.

47. (Withdrawn) A method of identifying at least one gene that either directly or indirectly suppresses telomerase activity, comprising, screening a cDNA or mRNA library generated from a senescent or near-senescent cell for members that suppress telomerase activity in an embryonic stem cell .

48. (Withdrawn) The method of Claim 47 whereby a decrease in telomerase activity is measured by measuring for decreased expression of a telomerase reporter gene.

49. (Withdrawn) The method of Claim 47 wherein said telomerase reporter gene is a construct comprising the hTRT gene fused to a reporter gene.

50. (Withdrawn) The method of Claim 49 wherein the construct comprises a gene fusion.

51. (Withdrawn) The method of Claim 49 wherein the construct comprises a protein fusion.

52. (Withdrawn) The method of Claim 47 whereby telomerase activity is decreased via a protein interaction, and a decrease in telomerase activity is measured via the TRAPeze assay.

53. (Withdrawn) The method of Claim 47 whereby said cDNA or mRNA library is subjected to subtractive hybridization with a cDNA or mRNA library from an embryonic stem cell prior to library screening

54. (Withdrawn) A method of identifying a protein that enhances telomerase activity, comprising

a. collecting fractions from the cytoplasm of an oocyte,

b. adding them to a cell-free system designed from a senescent or near-senescent cell, and

c. measuring for changes in telomerase activity that result from exposure to specific oocyte cytoplasmic fractions.

55. (Withdrawn) A gene identified by the method of Claim 40.

56. (Withdrawn) A gene identified by the method of Claim 47.

57. (Withdrawn) A protein identified by the method of Claim 54.

58. (Withdrawn) A method for screening for compounds that inhibit telomerase activity, comprising exposing an embryonic stem cell generated by nuclear transfer techniques using a senescent or near-senescent donor cell to a compound to determine whether said compound inhibits telomerase activity.

59. (Withdrawn) A compound identified by the method of Claim 58.

60. (Withdrawn) A pharmaceutical composition comprising the gene of Claim 55, or a portion or a transcription product thereof, for the purpose of enhancing telomerase activity in a subject in need of such enhanced activity.

61. (Withdrawn) A pharmaceutical composition comprising the gene product encoded by the gene of Claim 55 for the purpose of enhancing telomerase activity in a subject in need of such enhanced activity.

62. (Withdrawn) A pharmaceutical composition comprising the gene of Claim 56, or a portion or a transcription product thereof, for the purpose of suppressing telomerase activity in a subject in need of such suppressed activity.

63. (Withdrawn) A pharmaceutical composition comprising the gene product encoded by the gene of Claim 56 for the purpose of suppressing telomerase activity in a subject in need of such suppressed activity.

64. (Withdrawn) A pharmaceutical composition comprising the protein of Claim 58 for the purpose of enhancing telomerase activity in a subject in need of such enhanced activity.

65. (Withdrawn) A gene encoding the protein of Claim 58.

66. (Withdrawn) A pharmaceutical composition comprising the gene of Claim 65 for the purpose of enhancing telomerase activity in a subject in need of such enhanced activity.

67. (Withdrawn) A pharmaceutical composition comprising the compound of Claim 59 for the purpose of inhibiting telomerase activity in a patient in need of such decreased activity.

68. (Canceled)

69. (Previously presented) A rejuvenated cell produced according to the method of claim 1.

70. (Previously presented) A genetically-manipulated primary cell produced according to the method of claim 22.

71. (Previously presented) A re-cloned animal produced according to the method of claim 27.

72. (Previously presented) An inner cell mass produced according to the method of claim 29.

73. (Previously presented) A blastocyst produced according to the method of claim 29.

74. (Previously presented) A teratoma produced according to the method of claim 29.

75. (Previously presented) An embryo produced according to the method of claim 29.

76. (Previously presented) A fetus produced according to the method of claim 29.

77. (Previously presented) An animal produced according to the method of claim 29.

78. (Currently amended) A mammalian primary cell produced by the steps of:

a) transferring a mammalian donor cell, the nucleus from the mammalian donor cell, or at least one chromosome from the mammalian donor cell, to a recipient enucleated oocyte or enucleated egg in order to generate an embryo, wherein

the mammalian donor cell and the recipient oocyte or egg are derived the same mammalian species, and

the mammalian donor cell is a senescent cell or a near-senescent cell;

b) injecting an inner cell mass, an embryonic disc and/or a stem cell from the embryo into an immune-compromised animal to form a teratoma; and

c) isolating the mammalian primary cell from at least one of the germ layers of the teratoma.

79. (Canceled) ~~The primary cell of claim 78, wherein the donor cell is a senescent cell or a near-senescent cell.~~

80. (Previously presented) The primary cell of claim 78, wherein the primary cell comprises at least one telomere that is at least as long as a corresponding telomere of an age-controlled cell that is not produced by nuclear transfer.

81. (Previously presented) The primary cell of claim 78, wherein the primary cell comprises at least one telomere that is longer than a corresponding telomere of an age-controlled cell that is not produced by nuclear transfer.

82. (Currently amended) The primary cell of claim 78, wherein the mammalian donor cell of step (a) has at least one alteration to its genome prior to nuclear transfer.

83. (Previously presented) The primary cell of claim 82, wherein at least one of the genomic alterations of the donor cell comprises transfection of at least one heterologous gene or disruption of at least one native gene.

84. (Previously presented) The primary cell of claim 78, wherein the nuclear genotype of the primary cell is substantially the same as that of the donor cell.

85. (Previously presented) The primary cell of claim 78, wherein the primary cell is the same cell type as the donor cell.

86. (Previously presented) The primary cell of claim 78, wherein the primary cell is a different cell type than the donor cell.

87. (Previously presented) The primary cell of claim 78, wherein the donor cell type is selected from the group consisting of: smooth muscle, skeletal muscle, cardiac muscle, skin, and kidney.

88. (Previously presented) The primary cell of claim 78, wherein the primary cell type is selected from the group consisting of: smooth muscle, skeletal muscle, cardiac muscle, skin, and kidney.

89. (Previously presented) A tissue generated from the primary cell of claim 78.

90. (Previously presented) The tissue of claim 89, wherein the tissue is suitable for transplantation into a patient in need of a transplant of the tissue.

91. (Previously presented) The tissue of claim 90, wherein the donor cell is derived from the patient.

92. (Currently amended) A rejuvenated <u>mammalian</u> primary cell, wherein:

the rejuvenated mammalian primary cell is produced via nuclear transfer of a mammalian donor cell, wherein the mammalian donor cell is a senescent cell or a near-senescent cell; and

the rejuvenated primary mammalian cell comprises at least one telomere that is at least as long as a corresponding telomere of an age-controlled cell that is not produced by nuclear transfer.

93. (Canceled) ~~The primary cell of claim 92, wherein the donor cell is a senescent cell or a near senescent cell.~~

94. (Currently amended) The primary cell of claim 92, wherein the primary cell comprises at least one telomere that is longer than a corresponding telomere of [[an]] a same-age-controlled cell that is not produced by nuclear transfer.

95. (Currently amended) The primary cell of claim 92, wherein the donor cell, prior to nuclear transfer, has at least one alteration to the genome.

96. (Previously presented) The primary cell of claim 95, wherein at least one of the genomic alterations of the donor cell comprises transfection of at least one heterologous gene or disruption of at least one native gene.

97. (Currently amended) The primary cell of claim 92, wherein the nuclear genotype of the primary cell is ~~substantially~~ the same as that of the donor cell.

98. (Previously presented) The primary cell of claim 92, wherein the primary cell is the same cell type as the donor cell.

99. (Previously presented) The primary cell of claim 92, wherein the primary cell is a different cell type than the donor cell.

100. (Previously presented) The primary cell of claim 92, wherein the donor cell type is selected from the group consisting of: smooth muscle, skeletal muscle, cardiac muscle, skin, and kidney.

101. (Previously presented) The primary cell of claim 92, wherein the primary cell type is selected from the group consisting of: smooth muscle, skeletal muscle, cardiac muscle, skin, and kidney.

102. (Previously presented) A tissue generated from the primary cell of claim 92.

103. (Previously presented) The tissue of claim 102, wherein the tissue is suitable for transplantation into a patient in need of a transplant of the tissue.

104. (Previously presented) The tissue of claim 103, wherein the donor cell is derived from the patient.

105. (Previously presented) The primary cell of claim 92, wherein the primary cell is produced according to the steps of:

a) transferring the donor cell, the nucleus from the donor cell, or at least one chromosome from the donor cell, to a recipient oocyte or egg in order to generate an embryo;

b) injecting an inner cell mass, an embryonic disc and/or a stem cell from the embryo into an immune-compromised animal to form a teratoma; and

c) isolating the primary cell from at least one of the germ layers of the teratoma.